A request for a three-month extension of time to respond is included herewith. This three-month extension will bring the due date to May 20, 2002, which is within the six-month statutory period. Should such request or fee be deficient or absent, consider this paragraph such a request and authorization to withdraw the appropriate fee under 37 C. F. R. §§ 1.16 to 1.21 from Williams, Morgan & Amerson, P.C. Deposit Account No. 50-0786/4300.012700/MDM.

Reconsideration of the application in view of the following amendments and remarks is respectfully requested.

1. AMENDMENT

1.1 IN THE CLAIMS:

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Applicants formally cancel claims ~~38~~ 37, ~~39~~ 38, and ~~44~~ 43 to ~~77~~ 76 without prejudice and without disclaimer, as being drawn to the non-elected inventions.

Applicants also formally note election of polynucleotide species (Group I invention) that encode contiguous amino acid sequences from "SEQ ID NO:2" as required by the species election, and note that all pending claims read on the elected species.

Applicants note for the record that a clerical error in the numbering of the original claims has been identified. Claims were numbered 1-18 and then 20-77. On page 111 of the Specification it is noted that there is no claim numbered "19." For simplicity, Applicants propose to continue examination of the pending claims using original claim numbers, and simply note the inadvertent omission of claim 19 for the Examiner's record.

Please amend claims 1 and 9 to 13 to read as follows:

a1

1. (Amended) An isolated polynucleotide that:

(a) encodes a polypeptide having *S*-adenosyl-L-methionine:phosphoethanolamine *N*-methyltransferase activity and that comprises an at least 27 contiguous amino acid sequence from SEQ ID NO:2 or SEQ ID NO:4;

(b) encodes a polypeptide having *S*-adenosyl-L-methionine:phosphoethanolamine *N*-methyltransferase activity and at least about 85% sequence identity with the amino acid sequence of SEQ ID NO:2 or SEQ ID NO:4;

(c) comprises an at least 26 contiguous nucleotide sequence from SEQ ID NO:1 or SEQ ID NO:3; or

(d) hybridizes to the sequence of SEQ ID NO:1 or SEQ ID NO:3, or to the complement thereof, under stringent hybridization conditions.

a2

9. (Amended) The isolated polynucleotide of claim 1, comprising a sequence region that encodes a polypeptide having *S*-adenosyl-L-methionine:phosphoethanolamine *N*-methyltransferase activity and at least about 85% sequence identity with the amino acid sequence of SEQ ID NO:2 or SEQ ID NO:4.

Q2 cont.

10. (Amended) The isolated polynucleotide of claim 9, comprising a sequence region that encodes a polypeptide having *S*-adenosyl-L-methionine:phosphoethanolamine *N*-methyltransferase activity and at least about 90% sequence identity with the amino acid sequence of SEQ ID NO:2 or SEQ ID NO:4.

11. (Amended) The isolated polynucleotide of claim 10, comprising a sequence region that encodes a polypeptide having *S*-adenosyl-L-methionine:phosphoethanolamine *N*-methyltransferase activity and at least about 95% sequence identity with the amino acid sequence of SEQ ID NO:2 or SEQ ID NO:4.

12. (Amended) The isolated polynucleotide of claim 11, comprising a sequence region that encodes a polypeptide having *S*-adenosyl-L-methionine:phosphoethanolamine *N*-methyltransferase activity and at least about 96% sequence identity with the amino acid sequence of SEQ ID NO:2 or SEQ ID NO:4.

13. (Amended) The isolated polynucleotide of claim 12, comprising a sequence region that encodes a polypeptide having *S*-adenosyl-L-methionine:phosphoethanolamine

A2 cont. *N*-methyltransferase activity and at least about 98% sequence identity with the amino acid sequence of SEQ ID NO:2 or SEQ ID NO:4.

Please add the following new claims, 78-99:

--

A3 77 78. (New) The isolated polynucleotide of claim 7, comprising a sequence region that encodes a polypeptide having an at least 40 contiguous amino acid sequence from SEQ ID NO:2.

78 77 79. (New) The isolated polynucleotide of claim 78, comprising a sequence region that encodes a polypeptide having an at least 60 contiguous amino acid sequence from SEQ ID NO:2.

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79 78 80. (New) The isolated polynucleotide of claim 79, comprising a sequence region that encodes a polypeptide having an at least 80 contiguous amino acid sequence from SEQ ID NO:2.

80 79 81. (New) The isolated polynucleotide of claim 80, comprising a sequence region that encodes a polypeptide having an at least 100 contiguous amino acid sequence from SEQ ID NO:2.

Q13 Cont

82. (New) The isolated polynucleotide of claim 81, comprising a sequence region that encodes a polypeptide having an at least 120 contiguous amino acid sequence from SEQ ID NO:2.

83. (New) The isolated polynucleotide of claim 82, comprising a sequence region that encodes a polypeptide having an at least 140 contiguous amino acid sequence from SEQ ID NO:2.

84. (New) The isolated polynucleotide of claim 83, comprising a sequence region that encodes a polypeptide having an at least 160 contiguous amino acid sequence from SEQ ID NO:2.

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85. (New) The isolated polynucleotide of claim 1, comprising an at least 100 contiguous nucleotide sequence from SEQ ID NO:1 or SEQ ID NO:3.

86. (New) The isolated polynucleotide of claim 85, comprising an at least 120 contiguous nucleotide sequence from SEQ ID NO:1 or SEQ ID NO:3.

87. (New) The isolated polynucleotide of claim 86, comprising an at least 140 contiguous nucleotide sequence from SEQ ID NO:1 or SEQ ID NO:3.

Q3 cont

87 96
88. (New) The isolated polynucleotide of claim ~~87~~, comprising an at least 160 contiguous nucleotide sequence from SEQ ID NO:1 or SEQ ID NO:3.

88 87
89. (New) The isolated polynucleotide of claim ~~88~~, comprising an at least 180 contiguous nucleotide sequence from SEQ ID NO:1 or SEQ ID NO:3.

89 88
90. (New) The isolated polynucleotide of claim ~~89~~, comprising an at least 200 contiguous nucleotide sequence from SEQ ID NO:1 or SEQ ID NO:3.

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90 89
91. (New) The isolated polynucleotide of claim ~~90~~, comprising an at least 220 contiguous nucleotide sequence from SEQ ID NO:1 or SEQ ID NO:3.

91 90
92. (New) The isolated polynucleotide of claim ~~91~~, comprising an at least 240 contiguous nucleotide sequence from SEQ ID NO:1 or SEQ ID NO:3.

92 91
93. (New) The isolated polynucleotide of claim ~~92~~, comprising the nucleotide sequence of SEQ ID NO:1.

Cl 3 cont.

94. (New) The isolated polynucleotide of claim 91, comprising the nucleotide sequence of SEQ ID NO:3.

95. (New) An isolated polynucleotide that encodes a polypeptide having *S*-adenosyl-L-methionine:phosphoethanolamine *N*-methyltransferase activity and that comprises an at least 27 contiguous amino acid sequence from SEQ ID NO:2.

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96. (New) An isolated polynucleotide that encodes a polypeptide having *S*-adenosyl-L-methionine:phosphoethanolamine *N*-methyltransferase activity and at least about 85% sequence identity with the amino acid sequence of SEQ ID NO:2.

97. (New) An isolated polynucleotide that encodes a polypeptide having *S*-adenosyl-L-methionine:phosphoethanolamine *N*-methyltransferase activity, wherein said polynucleotide comprises an at least 26 contiguous nucleotide sequence from SEQ ID NO:1 or SEQ ID NO:3.

97. (New) An isolated polynucleotide that hybridizes to the sequence of SEQ ID NO:1 or SEQ ID NO:3, or to the complement thereof, under stringent hybridization conditions.

96. (New) An isolated polynucleotide comprising a sequence region that encodes a polypeptide having the sequence of SEQ ID NO:2.

2. RESPONSE

2.1 STATUS OF THE CLAIMS

Claims 1-77 were pending at the time of the action, and were subject to restriction and species election. Applicants previously elected to prosecute the DNAs, vectors, and host cells of Group I (claims 1-37 and 40-43), and elected as a species those polynucleotides that encode polypeptides having *S*-adenosyl-L-methionine:phosphoethanolamine *N*-methyltransferase activity and that comprise contiguous amino acid sequences from SEQ ID NO:2.

Claim 19 was inadvertently omitted due to a clerical error; therefore there is currently no pending claim 19. For clarity of examination, Applicants proceed with the original numbering, as the remaining claims and dependencies are correct.

Claims 38, 39, and 44-77 are canceled without prejudice and without disclaimer, as being drawn to non-elected inventions.

Claims 1 and 9-13 have been amended herein.

Claims 78 to 99 have been added herein and are entirely supported by the original disclosure.

Claims 1-37, 40-43, and 78-99, are therefore now pending in the case, and for the convenience of the Examiner, a copy of all pending claims including the present amendment is attached as Exhibit A.

Applicants note for the record that no rejections were entered for the pending claims, under 35 U. S. C. § 102, or 35 U. S. C. § 103, and as such, affirm the Examiner's position that the claims were free from any prior art concerns. Likewise, Applicants note for the record, and affirm the Examiner's position that no utility rejections under 35 U. S. C. § 101 exist for any of the pending claims.

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2.2 RESTRICTION/SPECIES/REJOINDER ISSUES

The Action Summary on page 1 (Item 4a) is in error in its statement that "claim(s) 14-39 and 44-77 is/are withdrawn from consideration." While it is true that claims 38, 39, and 44-77 have been cancelled as being drawn to non-elected inventions, this is not true for claims 14-37, which remain pending as drawn only to initially non-elected *species* within the elected Group I invention. In fact, as the present response confirms allowability of at least one generic claim (original claim 8, presented independently as claim 99) these claims (drawn to the originally non-elected species) must now be rejoined in the case.

The Action at page 2 also states that claims 1-13, and 40-43 are objected to for reciting limitations drawn to "non-elected inventions" (emphasis added). The Action's statement is incorrect. Claims 1-13 and 40-43 may encompass initially non-elected *species*; however, they do not encompass non-elected inventions, as they are all within the elected restriction group, the Group I claims. Moreover, as the Examiner notes that the subject matter of original dependent claim 8 (now presented in independent form as claim 99), at the very least, is now clearly in

condition for allowance, claims to the initially non-elected species must be rejoined in the case and examined.

The rule governing the treatment of species claims is set forth in 37 C.F.R. § 1.141(a). This rule provides, in pertinent part:

> "More than one species of an invention, not to exceed a reasonable number, may be specifically claimed in different claims in one national application, provided the application also includes an allowable claim generic to all the claimed species and all the claims to species in excess of one are written in dependent form (§ 1.75) or otherwise include all the limitations of the generic claim."

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For that reason and pursuant to 37 C. F. R. § 1.141(a), Applicants now formally request that the remaining claims in the Group I invention (claims 14-~~37~~ 36) be rejoined, and that all pending claims be examined on the merits in their entirety, following, for example, a search of the sequences identified in SEQ ID NO:1, SEQ ID NO:3, and SEQ ID NO:4.

Now that at least one generic claim is allowable, there is no proper mechanism for requiring the Applicants to restrict the claims only to the initially elected species. Rejoinder of each of the originally non-elected species is therefore proper and respectfully requested.

2.3 SUPPORT FOR THE CLAIMS

Support for amended and new claims is found throughout the original specification and claims as filed. Applicants certify that no new matter is introduced by the inclusion of these amendments.

Claims 1 and 9-13 have also been revised to further improve clarity in defining the subject matter, as the phrase "*S*-adenosyl-L-methionine:phosphoethanolamine *N*-methyltransferase" has replaced "PEAMT or ΔPEAMT" to more clearly describe one particular enzymatic activity encoded by certain polynucleotide species claimed in the invention,

namely *S*-adenosyl-L- methionine:phosphoethanolamine *N*-methyltransferase activity. Support for this amendment can be found throughout the Specification as filed, and particularly s[ecofoc written description may be found at least on page 2. For benefit of clarity, Applicants point the Examiner's attention to page 34 of the Specification where the legend to FIG. 2B indicates that the abbreviation "ΔPEAMT" has been used in the Specification to refer to those PEAMT-derived polypeptides that substantially lack two of the three N-methyltransferase activities (namely the methylation of P-MME to P-DME, and the methylation of P-DME to P-Cho) identified in the carboxyl region of the wild-type PEAMT polypeptide (see Specification at pages 89-90). The exemplary ΔPEAMT polypeptide identified in SEQ ID NO:4, is a truncation of the wild-type PEAMT sequence (SEQ ID NO:2) after the glycine residue at position 286. Both polypeptides, however, still possess *S*-adenosyl-L- methionine:phosphoethanolamine *N*-methyltransferase activity, and thus it is proper to describe them so, collectively in the pending claims.

Claim 12 has also been amended to rectify a clerical error. Support for the change is found throughout the original Specification and claims as filed, and particular written description support exists, for example, at least on pages 16-20.

Likewise, for clarity, and in anticipation of an Examiner interview to discuss particular aspects of the case, Applicants have voluntarily presented new independent claims 95-98, each directed to one of the four individual elements presented in the alternative in original claim 1. Applicants believe that entry of these new claims at this time will facilitate a cost-effective means for continuing prosecution on the merits, now that the remaining species will be rejoined and examined.

Finally, new claim 96 corresponds to previous dependent claim 8, now presented in its independent form, which was indicated to be allowable by the Examiner in the first Action.

2.4 THE REJECTION UNDER 35 U. S. C. § 112, 2ND PARAGRAPH, IS OVERCOME

Claims 9 to 13 have been rejected under 35 U. S. C. §112, 2nd paragraph, as being indefinite as allegedly failing to particularly point out and claim the subject matter that Applicants regard as their invention.

The Action rejects claims 9-13 as allegedly being indefinite in light of the "at least about" language in the claims, which the Examiner contends is a relative term that renders the claims indefinite. Applicants respectfully traverse. The use of both "relative terms" and particular claim language including the word "about" is perfectly acceptable under the law.

Applicants first respectfully point out that the Action has not actually set forth any reasoning to support the rejection. The rejection is thus *prima facie* improper. Applicants further respectfully point out that the rejection is at odds with long-established examination practice and case law and is therefore unsustainable.

Applicants have studied M. P. E. P. § 2173, concerning the criteria for assessing compliance with 35 U. S. C. § 112, second paragraph, and can find nothing to indicate that the present claims are indefinite by the use of terms including the phrase "at least about" (such as "at least about 85%," "at least about 95%", *etc.*). In fact, this section of the M. P. E. P. provides that Applicants can "define in the claims what they regard as their invention essentially in whatever terms they choose so long as the terms are not used in ways that are contrary to accepted meanings in the art" (M. P. E. P. § 2173.01, at page 2100-145, column 2). Clearly the term "about" in these claims is not used in a manner contrary to its ordinary meaning, and these claims are sufficiently definite and the rejection should be withdrawn.

M. P. E. P. § 2173.05 provides that claim language including "terms of degree" does not automatically render the claim indefinite. Rather, terms of degree are acceptable so long as one of ordinary skill in the art would be apprised of the scope of the claim. In order to determine whether a skilled artisan would understand a term of degree presented in a claim, this section of the MPEP indicates that the specification should be assessed in regard to the provision of "some standard for measuring that degree". Should such a standard be provided, the claims meet the requirements of 35 U. S. C. § 112, 2nd paragraph.

Only where the specification does not provide some standard for measuring the degree of a relative term, would a further inquiry be required. Even in such circumstances, M. P. E. P. § 2173.05 explains that the clarity requirements can still be met so long as one of ordinary skill in the art would nevertheless be reasonably apprised of the scope of the invention in view of the knowledge in the art. In fact, M. P. E. P. § 2173.05(b) specifically exemplifies that the term "about" is definite unless there is close prior art, or nothing in the specification, prosecution history, or prior art, to provide any indication as to what range the term "about" is applied to. In the present case, however, both the detailed standards for measurements set forth in the specification and the knowledge existing in the art support the definiteness of the pending claims.

For example, in rejected claim 9, the term "at least about 85% sequence identity", the word "about" is used both according to its ordinary dictionary definition and the common understanding in the biotechnological arts. Scientifically, one of ordinary skill in the art would understand the term "about 85%", as used in the claims and specification, to refer to its ordinary meaning, for example, "approximately 85%" (see the Specification at page 5, 12, and 16-20) would be understood to encompass those sequences that are approximately 85% identical, to the

recited sequence. Likewise, it would be clear to one of ordinary skill in the art that the term "about 95%", as used in the claims and specification, would also refer to its ordinary meaning, that is, sequences that are "approximately 95%" identical to the claimed sequence.

In light of the extremely detailed specification and the technical skill and knowledge in the art regarding determination of percent identity of two or more polynucleotide or polypeptide sequences, the present claims are sufficiently definite and the rejection should be withdrawn. If however, the Examiner still feels that such terms are indefinite, Applicants could nevertheless elect to introduce claim language that reads "at least 85% identical," "at least 86% identical" "at least 87% identical," "at least 88% identical," "at least 89% identical" *etc.*, as there is specific written description for such amendment in the Specification, particularly at least on page 16, first paragraph.

Finally, for the record, Applicants also note that the rejected claim language has been used extensively in the molecular biology art units, and particularly when describing "at least about XX%" sequence identity or homology in amino acid and/or polynucleotide inventions. In fact, a search of the patent database reveals no less than four-dozen patents have been issued within the past 4 years that employ this specific language (see *e.g.*, U. S. Patents 6,359,197 [claims 1 and 3]; 6,388,052 [claims 17 and 18]; 6,372,475 [claims 1 and 2]; 6,365,364 [claim 1]; and 6,087,122 [claims 1 to 3], *etc.*).

Applicants believe this fully addresses the concerns of the Examiner with respect to clarity of these claims and request that the rejection be withdrawn.

2.5 THE REJECTIONS UNDER 35 U. S. C. § 112, 1ST PARAGRAPH, ARE OVERCOME

Claims 1-7 and 9-13 and 40-43 were rejected under 35 U. S. C. §112, 1st paragraph, (a) allegedly for containing subject matter which was not described in the specification in such as way as to enable one of skill in the art to make and/or use the invention; and (b) because the Specification allegedly is enabling only for a spinach PEAMT sequence (SEQ ID NO:2).

Applicants respectfully traverse each of these rejections.

Although Applicants contest the rejection as applied to claims 1-7, 9-13, and 40-43, the indication of subject matter already agreed to be fully enabled (*e.g.*, the subject matter of claim 8) is appreciated. In fact, the indication that claim 8 is fully enabled compels a finding of adequate enabling support for certain of the rejected claims.

The rejection of these claims appears to rest on the allegation that the specification does not reasonably enable all DNA segments that encode polypeptides having *S*-adenosyl-L-methionine:phosphoethanolamine *N*-methyltransferase activity and that have at least about 27 contiguous amino acids in common with the recited species (SEQ ID NO:2 and SEQ ID NO:4) (Action bridging pages 3 and 4). The Action appears to argue that not all species within the claimed genus would possess *S*-adenosyl-L-methionine:phosphoethanolamine *N*-methyltransferase enzymatic activity. That is in fact, a correct statement. Because the language of claim 1 is presented in the alternatively, only a subset of the claimed polynucleotide species need encode an enzymatically-active *S*-adenosyl-L-methionine:phosphoethanolamine *N*-methyltransferase protein (*e.g.*, those falling within the scope of elements (a) or (b). Not every claimed polynucleotide need encode a functional protein. In fact, many of the claimed polynucleotides may be used as primers to identify other *S*-adenosyl-L-methionine:phosphoethanolamine *N*-methyltransferase-encoding homologous

nucleic acid sequences. Others, for example, may encode only portions of the *S*-adenosyl-L-methionine:phosphoethanolamine *N*-methyltransferase protein sequences, such as, for example, those used to generate peptide epitopes, or those used to purify *S*-adenosyl-L-methionine:phosphoethanolamine *N*-methyltransferase-specific antibodies. In fact, the polynucleotides of the claimed invention may be used in a variety of diagnostic and recombinant methodologies without these sequences encoding fully-functional *S*-adenosyl-L-methionine:phosphoethanolamine *N*-methyltransferase polypeptides or proteins. This fact does not make these polynucleotide sequences undesirable, nor does it render these species unpatentable.

Respectfully, Applicants point out firstly that only two members of the Markush language of claim 1 [elements (a) and (b)] require the claimed polynucleotides to encode a protein (either an enzymatically-functional one, or a non-enzymatically-functional one, such as for example, peptide epitopes useful in the production of *S*-adenosyl-L-methionine:phosphoethanolamine *N*-methyltransferase-specific antibodies. The alternative elements in claim 1 recite that the claimed polynucleotides need only (c) comprise a sequence of at least 26 contiguous nucleotides of SEQ ID NO:1 or SEQ ID NO:3, or (d) hybridize to the sequence of SEQ ID NO:1 or SEQ ID NO:3 or to the complement thereof under stringent hybridization conditions.

The essence of this rejection apparently lies in the assertion that no guidance is provided on how to obtain or identify a nucleotide sequence that encodes a polypeptide having *S*-adenosyl-L-methionine:phosphoethanolamine *N*-methyltransferase enzymatic activity, wherein the polypeptide comprises an at least 27 contiguous amino acid sequence from SEQ ID NO:2 or SEQ ID NO:4 (Action at middle of page 4), and the requirements for guidance on functional enzymes and working examples on "enzymatically active"

S-adenosyl-L-methionine:phosphoethanolamine *N*-methyltransferase-encoding polynucleotides besides those present in the Examples (Action, pages 5 and 6). These apparent standards for patentability (and the underlying assessment of enabling support) include various fundamental flaws, which are addressed in the following sections.

2.5.1 THE POLYNUCLEOTIDES OF THE INVENTION NEED NOT ENCODE ENZYMATICALLY-ACTIVE PEAMT PROTEINS

The Action's focus on the "an at least 27 contiguous amino acid sequence from SEQ ID NO:2 or SEQ ID NO:4" of element (a) of claim 1, or the "at least about 85% sequence identity with the amino acid sequence of SEQ ID NO:2 or SEQ ID NO:4" of element (b) of claim 1, overlooks the fundamental requirement that polypeptides falling within the scope of these 2 elements of the claim encompass polynucleotides that encode a protein or peptide that possesses *S*-adenosyl-L-methionine:phosphoethanolamine *N*-methyltransferase activity. The sequence recitations are present in elements (a) and (b) the claims to add supplementary structural features for further definition of the claimed polynucleotides. Likewise, the sequence recitations present in elements (c) and (d) of claim 1 also adds supplementary structural features for further definition of the claimed polynucleotides. This sequence information cannot be interpreted in a vacuum, but read in light of the Specification. *Slimfold Mfg. Co. vs. Kinkead Industries, Inc.*, 1 USPQ 2d 1563 (Fed. Cir. 1987). Therefore, Examination of Claim 1 cannot simply focus on those polynucleotide sequences that ONLY possess the required elements present in (a) and (b), namely that the claimed polynucleotides encode a product that has *S*-adenosyl-L-methionine:phosphoethanolamine *N*-methyltransferase enzymatic activity.

However, for those species of the claimed genus, the specification includes detailed guidance on what constitutes a polypeptide, protein, or peptide that possesses "PEAMT" enzymatic activity. In addition to the primary sequence information, the detailed guidance includes substantial information on its isolation and purification characteristics, molecular weight, *etc.*

In light of such details, one of ordinary skill in the art would clearly be able to make and use a DNA segment that encodes a *S*-adenosyl-L-methionine:phosphoethanolamine *N*-methyltransferase protein, polypeptide, or peptide without undue experimentation. The present rejection should be overcome on this basis alone. The specification "*must* be taken as in compliance with the enabling requirement of the first paragraph of § 112 *unless* there is reason to doubt the objective truth of the statements". *In re Marzocchi & Horton*, 169 USPQ 367 (CCPA 1971); emphasis as in original.

2.5.2 How to "Make and Use" The Polynucleotides of the Invention

The Action appears to have overlooked the practical requirements of utility and enablement. Any practical usefulness is sufficient to satisfy the utility requirement of § 101 and the "how to use" requirement of § 112, first paragraph. *Cross v. Iizuka*, 224 USPQ 739, 748 (Fed. Cir. 1985); *In re Brana*, 34 USPQ 2d 1436 (Fed. Cir. 1995).

The claimed DNA segments have numerous practical uses outside recombinant expression, and outside the production of enzymatically-active proteins. For example, these polynucleotides find particular use in various hybridization and cloning embodiments. Where the polynucleotides segments are used in recombinant expression, there is absolutely no requirement that the expressed protein or polypeptide be enzymatically active. The requirements are only that a skilled artisan be

able to make and use the DNA segments without undue experimentation (§ 112, first paragraph) and that the product have some practical utility (§ 101).

The Action does not question the ability of an artisan to practice recombinant expression techniques, so the § 112 requirement is clearly met. Likewise, claims directed to polynucleotides that encode *S*-adenosyl-L-methionine:phosphoethanolamine *N*-methyltransferase-derived peptides and or proteins, also meet the § 101/§ 112 requirements, because such peptides and polypeptides (as well as the polynucleotides encoding them) may be used in various embodiments that do not require *S*-adenosyl-L-methionine:phosphoethanolamine *N*-methyltransferase enzymatic activity. For example, the Specification notes on pages 11 bridging to 12 that various uses for *S*-adenosyl-L-methionine:phosphoethanolamine *N*-methyltransferase proteins/peptides lacking enzymatic activity, including for example, as controls in activity studies; to bind and purify counterpart *S*-adenosyl-L-methionine:phosphoethanolamine *N*-methyltransferase-specific antibodies; to generate *S*-adenosyl-L-methionine:phosphoethanolamine *N*-methyltransferase-specific peptide epitopes, to immunize animals to produce *S*-adenosyl-L-methionine:phosphoethanolamine *N*-methyltransferase-specific antibodies, and to purify proteins that interact with *S*-adenosyl-L-methionine:phosphoethanolamine *N*-methyltransferase-derived peptides, polypeptides, or proteins, among other things.

Moreover, the Specification exhaustively teaches how to make and use such *S*-adenosyl-L-methionine:phosphoethanolamine *N*-methyltransferase compositions in a variety of *in vivo* and *in vitro* embodiments, including the generation of recombinant host cells and transgenic plants that comprise one or more of the claimed polynucleotide compositions. In fact, from page 12 to page 33, there is extensive written description on using the claimed

polynucleotides in a variety of embodiments. Importantly, any experimentation required in the practice of these embodiments, would thus be confined to very routine matters of protein and antibody production and the use of such compositions in functional assays or cell transformation experiments, each of which is described at length in the specification.

Should any experimentation be necessary, it would certainly not rise to the level of "undue experimentation". In assessing the question of whether undue experimentation would be required, the key term is "undue", not "experimentation". *In re Angstadt and Griffin*, 190 USPQ 214 (C. C. P. A. 1976). The need for some experimentation does not render the claimed invention unpatentable under 35 U. S. C. § 112, 1st paragraph. Indeed, a considerable amount of experimentation may be permissible if such experimentation is routinely practiced in the art. *In re Angstadt and Griffin, supra.*

The issue in this case is similar to that decided by the Federal Circuit in *In re Wands*, 8 U.S.P.Q.2d 1400 (Fed. Cir. 1988) (although any experimentation in the present case should be less than in *Wands*). In *Wands*, the P.T.O. took the position that the applicant failed to demonstrate that the disclosed biological processes of immunization and antibody selection could reproducibly result in a useful biological product (antibodies from hybridomas) within the scope of the claims. In its decision overturning the P.T.O.'s rejection, the Federal Circuit found that Wands' demonstration of success in four out of nine cell lines screened was sufficient to support a conclusion of enablement. The court emphasized that the need for some experimentation requiring, *e.g.*, production of the biological material followed by routine screening, was not a basis for a finding of non-enablement, stating:

> "Disclosure in application for the immunoassay method patent does not fail to meet enablement requirement of 35 USC 112 by requiring 'undue experimentation,' even though production of monoclonal antibodies necessary to practice invention first requires production and screening of numerous antibody

producing cells or 'hybridomas,' since practitioners of art are prepared to screen negative hybridomas in order to find those that produce desired antibodies, since in monoclonal antibody art one 'experiment' is not simply screening of one hybridoma but rather is entire attempt to make desired antibody, and since record indicates that amount of effort needed to obtain desired antibodies is not excessive, in view of Applicants' success in each attempt to produce antibody that satisfied all claim limitations."

8 U.S.P.Q.2d at 1400.

The parallels between *Wands* and the present case are striking. Practice of the presently claimed invention does not require undue experimentation, even though the production of various polynucleotides and/or polypeptides "may" require screening to confirm activity, or may involve comparing the DNA or protein sequence of a candidate species to those sequences disclosed, for example, in SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, and/or SEQ ID NO:4. Practitioners in the art routinely conduct functional screening assays and DNA and protein sequence determination and comparison. Such comparisons and determinations, clearly is not undue experimentation.

2.5.3 BREADTH OF DISCLOSED EXAMPLES

The Action at the bottom of page 6 argues that there is unpredictability is selecting DNA sequences that encode proteins that express PEAMT activity, and that "the lack of working examples other than SEQ ID NO:2" renders the claimed invention unpatentable. Again, Applicants respectfully traverse. The Specification clearly discloses how to isolate, identify, characterize, synthesize, and assay a family of polynucleotides that (a) encode *S*-adenosyl-L-methionine:phosphoethanolamine *N*-methyltransferase-specific proteins, polypeptides, or peptides that share sequence identity with a contiguous sequence region from one or more disclosed sequences (*e.g.*, SEQ ID NO:2 and SEQ ID NO:4); (b) encode

S-adenosyl-*L*-methionine:phosphoethanolamine *N*-methyltransferase-specific proteins, polypeptides, or peptides that have at least about 85% sequence identity to one or more disclosed polypeptide sequences (*e.g.*, SEQ ID NO:2 and SEQ ID NO:4); (c) comprise at least 26 contiguous nucleotides from SEQ ID NO:1 or SEQ ID NO:3; or (d) hybridize to the sequence of SEQ ID NO:1 or SEQ ID NO:3.

Clearly the "make and use" requirement and the specific written description requirement for these species have been satisfied, and the breadth of the working examples is entirely commensurate with the scope of the claims. Therefore, the 35 U. S. C. § 112, 1st paragraph rejection as a whole is overcome, and should be withdrawn.

2.6 REQUEST FOR EXAMINER INTERVIEW

Because of the complex nature of biotechnology inventions, and the progress already achieved as evidenced by allowable subject matter at the first Action, Applicants hereby request the granting of an Interview between Examiner McElwain and Applicants' undersigned representative, Dr. Mark D. Moore, pursuant to M. P. E. P. § 713.01 and 37 C. F. R. §1.133, to discuss the pending claims and to clarify any particular remaining issues that may be in the mind of the Examiner, once she has had the opportunity to review this response and accompanying amendment. To that end, Applicants' undersigned representative will telephone Examiner McElwain within the next 30 days to schedule such interview at a time that is mutually agreeable to both parties.